

## **Football as Medicine: Prescribing football for global health promotion”**

A Routledge Book published within the book series: Critical Research in Football

Edited by Professor Peter Krstrup<sup>1</sup> and Dr Daniel Parnell<sup>2</sup>

<sup>1</sup> University of Southern Denmark, Odense, Denmark, <sup>2</sup> University of Liverpool Management School, University of Liverpool, Liverpool, United Kingdom.

### **CHAPTER 3: FOOTBALL FOR PROMOTION OF BONE HEALTH ACROSS LIFESPAN.**

**DIMITRIS VLACHOPOULOS<sup>1</sup>, CRAIG A. WILLIAMS<sup>1</sup>, EVA WULFF HELGE<sup>2</sup>,  
PER AAGAARD<sup>3</sup>, NIKLAS RYE JØRGENSEN<sup>4,5</sup>, PETER KRUSTRUP<sup>2,3</sup>.**

<sup>1</sup>Children’s Health and Exercise Research Centre, Sport and Health Sciences, University of Exeter, Heavitree Road, EX1 2LU, Exeter, UK;

<sup>2</sup>University of Copenhagen, Department of Nutrition, Exercise and Sports, Nørre Allé 51, 2200 Copenhagen N, Denmark.;

<sup>3</sup>Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Campusvej 55, Odense, DK-5230, Denmark;

<sup>4</sup>Department of Clinical Biochemistry, Rigshospitalet, Valdemar Hansens Vej, 2600 Glostrup, Denmark

<sup>5</sup>OPEN, Odense Patient data Explorative Network, Odense University Hospital/Institute of Clinical Research, University of Southern Denmark, J.B.Winsløws Vej, 5000 Odense, Denmark

Dimitris Vlachopoulos: [D.Vlachopoulos@exeter.ac.uk](mailto:D.Vlachopoulos@exeter.ac.uk)

Craig A. Williams: [C.A.Williams@exeter.ac.uk](mailto:C.A.Williams@exeter.ac.uk)

Eva Wulff Helge: [ewhelge@nexs.ku.dk](mailto:ewhelge@nexs.ku.dk)

Per Aagaard: [PAagaard@health.sdu.dk](mailto:PAagaard@health.sdu.dk)

Niklas Rye Jørgensen: [niklas@dadlnet.dk](mailto:niklas@dadlnet.dk)

Peter Krstrup: [pkstrup@health.sdu.dk](mailto:pkstrup@health.sdu.dk)

## **Abstract**

The prevalence of osteoporosis and fragility fractures is expected to increase due to the increasing life expectancy of the population worldwide. Determinants of osteoporosis include the genetic predisposition and environmental factors, such as exercise and diet that can affect peak bone mass attainment. Peak bone mass is achieved between the second and third decade of life, with 80-90 % acquired by late adolescence followed by a decrease of approximately 1% annually from the fifth decade of life. Weight-bearing exercise has an important role on bone development and maintenance of skeletal bone mass due to the mechanical loads produced and the repetitive forces applied on the skeleton. Football includes a wide variety of intermittent high-intensity movements, which produce large ground reaction forces that can stimulate bone formation and skeletal adaptations. Cross-sectional, longitudinal and randomised controlled trials have been conducted to investigate the impact of football participation on skeletal bone health during developmental growth and in adulthood. Evidence indicates that football exercise can have positive effects on bone development and structure in both male and female children and adolescents. During adulthood football participation can maintain and improve bone health in untrained, healthy as well as middle-aged and older men and women including various clinical patient groups with evidence indicating structural, cellular and clinical relevant bone adaptations. The skeletal benefits are site-specific and adaptations are observed particularly at the skeletal regions stimulated by mechanical loads. Concluding this chapter is a focus on the scientific evidence indicating that football participation is an effective strategy to promote bone health during childhood, adolescence and in adulthood.

## **Keywords**

Bone health, football participation, osteoporosis, health promotion

## **Author bios**

Dr Dimitris Vlachopoulos is Lecturer in Sport and Health Sciences of University of Exeter. He is part of Children's Health and Exercise Research Centre group and his research is focusing on exercise and musculoskeletal development during growth.

Professor Craig A. Williams is Director of the Children's Health and Exercise Research Centre. He is an internationally recognised expert on paediatric exercise physiology and his research work focuses on the physiological responses of exercise training of young people.

Associate Professor Eva Wulff Helge is head of studies in exercise and sport sciences at the University of Copenhagen. Her main research interest is health promotion through exercise and sports, with a specific focus on preventing and treating osteoporosis. The need for translational and cross-disciplinary research with a synergetic coupling between theory and practice is highly acknowledged.

Dr. Per Aagaard is Professor in Biomechanics at the Department of Sports Science and Clinical Biomechanics, Muscle Physiology and Biomechanics Research Unit, University of Southern Denmark. His research is focusing on the adaptive plasticity in neuromuscular function and muscle morphology/architecture with exercise training in young and old adults, including the collateral effects on musculoskeletal health.

Professor Niklas Rye Jørgensen is head of Section of Clinical Biochemistry at Rigshospitalet Glostrup and professor at Institute of Clinical Research at The University of Southern Denmark. His research is focusing on the biochemical markers of bone turnover and on the biological effects of loading on bone and bone cells.

## Figures and Tables

**Figure 1.** Changes in BMC with 3 years of football training in young footballers (9 to 12 years) for the whole femur and femoral regions after adjustment for the concurrent increase in age, height, and body mass. Adapted from (Vicente-Rodriguez et al. 2004).

**Figure 2.** Percentage change in total volumetric BMD in distal tibia for untrained premenopausal women after 14 weeks of training football (n=12), running (n=16) and an inactive lifestyle (n=9). Results from the left leg are shown in black and results from the right leg in grey. Means  $\pm$  standard deviation. \* denotes significant difference from running and control groups ( $P < 0.05$ ), # denotes significant difference from control group ( $P < 0.05$ ). Adapted from (Helge et al. 2010).

## **Table of Contents**

### 3.1 Introduction

### 3.2 Football participation for promotion of bone health during growth

#### 3.2.1 Cross-sectional studies on football and bone health during growth

#### 3.2.2 Longitudinal studies on football and bone health during growth

#### 3.2.3 Football and structural bone adaptations during growth

### 3.3 Football participation for promotion bone health during adulthood

#### 3.3.1 Cross-sectional studies on football and bone health during adulthood

#### 3.3.2 Acute and long terms skeletal adaptations from football during adulthood

#### 3.3.3 Football participation and cellular bone adaptations during adulthood

### 3.4 Conclusions

### 3.1 Introduction

Osteoporosis is characterized by compromised bone strength predisposing a person to an increased risk of fracture (NIH Consensus Development Panel on Osteoporosis Prevention and Therapy 2001). Approximately 200 million people are affected by osteoporosis worldwide and in the European Union, 22 million women and 5.5 million men are estimated to have osteoporosis (Hernlund et al. 2013). The prevalence of osteoporosis is expected to increase due to an aging population (Reginster and Burlet 2006) and the world population  $\geq 65$  years of age is predicted to double from about 506 million in 2008 to 1.3 billion by 2040, at which time it will account for 14 % of the world's total population (Kinsella and Wan 2008). The economic burden of osteoporosis in Europe is higher than most types of cancer (except lung cancer), or chronic cardiorespiratory diseases (Kanis et al. 2008, Johnell and Kanis 2006) and represents a direct annual cost of  $\sim$  €31.7 billion to health care and social services (Kanis and Johnell 2005). Approximately 30 % of all postmenopausal women have osteoporosis in the United States and in Europe and at least 40 % of these women and 15-30 % of men will sustain one or more fragility fractures in their remaining lifetime. The economic burden of incident and prior fragility fractures are estimated at €37 billion, and due to the aging of the population, the costs are expected to increase by 25 % in 2025 (Hernlund et al. 2013). Approximately 20 % of all patients with a hip fracture do not survive for more than 1 year from diagnosis and more than 50 % never completely regain their previous functional status (Boonen et al. 2005). The increased mortality and morbidity, physical disabilities and chronic pain after fractures can lead to loss of independence, hence primary prevention remains the most important policy action in public health to reduce the prevalence of osteoporosis and fractures.

Determinants of osteoporosis include a high genetic component with epidemiological studies indicating that heritable factors account for 60-80 % of the variability in bone mineral density (BMD) and bone mineral content (BMC) (Mitchell et al. 2015, Stewart and Ralston

2000, Bachrach 2001), while environmental and modifiable factors (e.g. calcium, vitamin D and exercise) (Courteix et al. 2005, Ward et al. 2007, Lappe et al. 2014, Mouratidou et al. 2013, Valtuena et al. 2012, Vlachopoulos et al. 2016) account for the remaining BMD variance. Peak bone mass (PBM) attainment typically occurs between the second and third decade of life, with 80-90 % acquired by late adolescence, although this is dependent on the specific skeletal site (Baxter-Jones et al. 2011, Henry, Fatayerji, and Eastell 2004). During the years of puberty, girls acquire approximately 40 % of their PBM, meaning they had achieved approximately 90 % of PBM by the age of 18 (Theintz et al. 1992). The PBM is relatively stable until the onset of bone loss with aging. In addition to the age-related bone loss for both men and women, women experience an accelerated loss for 3-6 years at menopause (Faulkner and Bailey 2007). Moderate to vigorous physical activity (MVPA) contributes to achieving the full potential of PBM (Gordon et al. 2017), which is an important predictor for BMD in elderly and hence, maximising the PBM may be essential prevention strategy for reducing the incidence and prevalence of osteoporosis.

Exercise is well known to play an important role in bone development and maintenance of bone mass due to the mechanical loads produced and the repetitive forces applied on the skeleton that trigger bone modeling and remodeling (Wolff et al. 1999). It has been suggested that short-duration and high intensity loading movements of a sufficient magnitude stimulate bone cell activity and induce bone adaptations that lead to increased bone strength (Turner 1998). The relationship between muscle and bone led to the functional “bone-muscle unit” theory, suggesting that long-term changes in muscle strength (either increased or decreased) affects bone strength linearly (Schoenau and Frost 2002). According to the potential to augment bone mass and geometry during growth, exercises can be categorized as osteogenic (weight-bearing and high-intense exercise) or non-osteogenic (non-weight-bearing and low-intense exercise) (Courteix et al. 1998, Bass et al. 2002, Duncan et al. 2002, Faulkner et al. 2003, Ward

et al. 2005, Tournis et al. 2010, Dowthwaite, Rosenbaum, and Scerpella 2012, Ferry et al. 2013, Maimoun et al. 2013). Training including weight-bearing activities, may elicit greater improvements in BMC and BMD than non-weight bearing activities, while non-weight bearing activities may have no osteogenic effect or even inflict a negative effect on bone development in children and adolescents (Hind and Burrows 2007). Considering that the majority of children and adults in developed countries are participating in sports during growth and adulthood, it is important to understand how participation in different loading sports can promote bone health and reduce the prevalence of osteoporosis and the incidence of fractures.

Football is the most popular sport worldwide with around 300 million registered football players worldwide accounting for approximately 4% of the world's total population (Dvorak and Junge 2015). Football includes intermittent high-intensity movements, involving various types of runs, multiple and rapid changes of directions, accelerations and decelerations, jumps and kicks, which produce large ground reaction forces that can stimulate bone formation and skeletal adaptations during childhood and adolescence (Ara et al. 2006, Vicente-Rodriguez et al. 2004, Krstrup et al. 2010, Calbet et al. 2001). Additionally, football training can improve bone health outcomes during adulthood, including untrained populations (Helge et al. 2010), clinical populations (Uth et al. 2018), women (Krstrup et al. 2010, Jackman et al. 2013) and men (Helge, Andersen, et al. 2014, Hagman et al. 2018). Cross-sectional and longitudinal studies investigating the effect of football participation on bone health during growth and in adulthood have mainly used dual-energy X-ray absorptiometry (DXA) (Hagman et al. 2018, Vicente-Rodriguez et al. 2004, Jackman et al. 2013) and geometry estimates, such as hip structural analysis (HSA) (Nikander et al. 2005, El Hage 2013) and trabecular bone score (TBS) (Vlachopoulos, Barker, Ubago-Guisado, et al. 2017, Heinio, Nikander, and Sievanen 2015), but there are also studies that included peripheral quantitative computed tomography (pQCT) (Helge et al. 2010), Quantitative Ultrasound (QUS) (Torres-Costoso et al. 2018, Falk



et al. 2010) and bone turnover markers (Mohr et al. 2015, Weiler, Keen, and Wolman 2012, Helge, Randers, et al. 2014). This chapter will comprehensively outline the role of football participation to promote bone health across the lifespan and reduce the prevalence of osteoporosis and non-traumatic fractures.

### **3.2 Football participation for promotion of bone health during growth**

#### **3.2.1 Cross-sectional studies on football and bone health during growth**

During developmental growth, participation in football positively affects bone mass in both genders in children and adolescents according to a recent systematic review and meta-analysis (Lozano-Berges et al. 2018). Their meta-analysis indicated that the mean differences in total body BMD between soccer players and sedentary controls were 0.061 (95% CI, 0.042–0.079) in males and 0.063 (95% CI, 0.026–0.099) in females (Lozano-Berges et al. 2018). Additionally, the effects of football practise on BMD were greater during pubertal years compared to pre-pubertal years (Lozano-Berges et al. 2018). Cross-sectional data in prepubescent male footballers demonstrate that long-term football participation for at least 3 hours per week leads to greater BMC at the lumbar spine, femoral neck and trochanter skeletal sites compared to that observed in non-athletic controls (Vicente-Rodriguez et al. 2003) (**Figure 1**), which indicates that the effects of football practise on skeletal bone health may be evident when practicing at least 3 hours training per week, however it should be noted that the optimal volume of football training for osteogenic stimulus has not been established yet. A recent cross-sectional study found that adolescent male footballers had significantly higher BMD (8.8 % to 25.1 %) and BMC (7.9 % to 29.5 %) than active controls at all sites of the skeleton except for the lumbar spine and arms after adjusting for age, height, region-specific

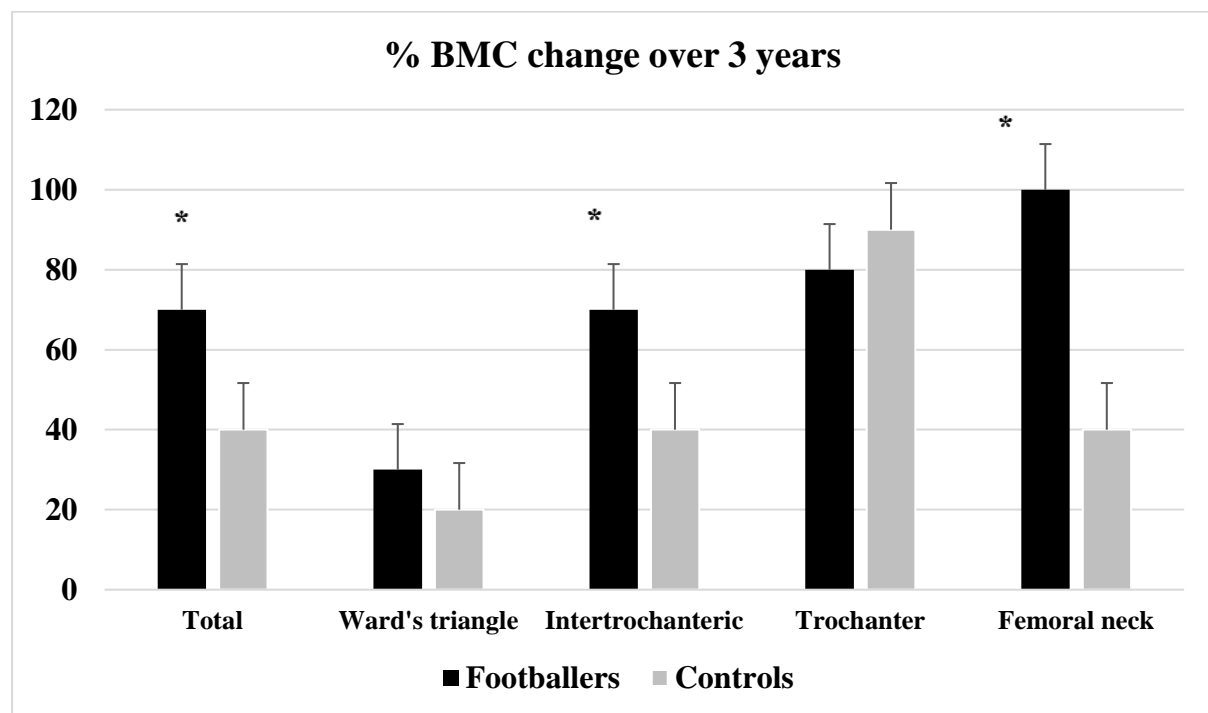
lean mass, calcium intake and MVPA (Vlachopoulos, Barker, Williams, et al. 2017). A comparison between adolescent female swimmers and footballers found that swimmers had significantly lower BMD at all body sites compared to footballers, while also showing lower values compared with untrained age-matched controls (Ferry et al. 2011). Site specific adaptations from football practise were investigated by Seabra et al. that found total body BMD and lower limb BMD at dominant and non-dominant site were substantially higher in footballers compared to controls after controlling for maturity offset. However, no significant differences were found for BMC (Seabra et al. 2013). Nebigh et al. showed similar results in pubertal but not in pre-pubertal male football players compared to controls (Nebigh et al. 2009). Moreover, Silva et al. showed that male adolescent footballers had significantly higher hip BMD than controls at the end of puberty (16–18 years), and that footballers at the end of puberty had higher total body, lumbar spine and proximal femur BMD than footballers at the initial age of puberty (10–12 years) (Silva et al. 2011). These findings can be explained by the greater muscle strength of young footballers, which was found to be the strongest predictor of bone mass and structure (Vlachopoulos, Ubago-Guisado, et al. 2017, Vicente-Rodriguez et al. 2005). Notably, the magnitude of the differences reported among various studies appears to arise from the use of different confounders (e.g. height, lean mass, hours of training and nutritional intakes) and highly differing characteristics of study participants (e.g. sexual maturation status).

### **3.2.2 Longitudinal studies on football and bone health during growth**

Longitudinal studies evaluating the effect of football participation on bone health during childhood and adolescence are limited, and a study performed by Agostinete et al. found no BMD accrual differences between young football players and controls after 9 months of

football training (Agostinete et al. 2016). However, following 1 year of football training no differences in BMD and BMC could be noted between the football group and the active controls after adjusting for baseline bone status, age, height, lean mass, MVPA and maturity (Vlachopoulos et al. 2018). A study conducted by Zouch et al. found no differences between footballers and controls at baseline, but after 10 months of football training there were significant improvements in BMC at whole body, lumbar spine, total hip, and lower limbs compared to controls, with amplified increases observed in those who trained for 4 hours per week compared with individuals who trained for 2 hours per week (Zouch et al. 2008). After 1 year of football training the pubertal football players demonstrated higher BMC compared to controls. After 1 year, greater increases in BMC at whole body, total hip, and lower limbs were observed for pre-pubertal football players compared to controls, whereas pubertal players also showed greater increases at lumbar spine BMC. When both groups of football players were compared, greater BMC increases were reported in pubertal players than in pre-pubertal players (Zouch et al. 2014). Also, it was noted that the bone gains were greater when evaluated for the total body and weight-bearing bones (the lumbar spine, total hip, and supporting leg) compared to non-weight-bearing bones (dominant arm and non-dominant arm) in boys who became pubescent during the 1 year study period. No differential gains were observed in boys who remained prepubescent (Zouch et al. 2014). After 3 years of football training football players showed larger BMC and BMD gains at for whole body, lumbar spine, total hip, and lower limbs compared to non-exercising controls (Zouch et al. 2015). Another study followed 9-year-old male footballers for 3 years and compared selected bone health parameters with that of controls (**Figure 1**). Their data revealed that footballers gained twice as much femoral neck and intertrochanteric BMC than the control group and their mean hip BMD increased 33% more than the control group (Vicente-Rodriguez et al. 2004). Likewise, muscle-skeletal structures were found to respond positively to the weight-bearing and impact-loading imposed by

football practice (Seabra et al. 2013) and enhancement of lean mass was found to be the best predictor of this bone mass accumulation during growth (Vicente-Rodriguez et al. 2005).



**Figure 1.** Changes in BMC with 3 years of football training in young footballers (9 to 12 years) for the whole femur and femoral regions after adjustment for the concurrent increase in age, height, and body mass. Adapted from (Vicente-Rodriguez et al. 2004).

Randomised controlled trials allocating only football to improve musculoskeletal outcomes during growth have not been conducted, however a recent 10-month school-based intervention in children aged 8-10 years compared the musculoskeletal effects of small-sided ball games and circuit strength training for 40 minutes 3 times per week. The small-sided ball game training consisted of 75% 3x3 football training and 25% of 3v3 basketball and floorball games. The study showed that the small-sided ball game group significantly improved total body BMD and leg BMC compared to age-matched controls, and had significantly higher change in leg BMD compared with controls and the circuit strength training group. These findings indicate that small-sided ball games, mainly football, can improve bone mineralisation and could be implemented in the school system (Larsen et al. 2018).

### **3.2.3 Football and structural bone adaptations during growth**

In addition to BMD and BMC gains, exercise can also influence the structural bone outcomes (Hind et al. 2012). A combination of bone quantity, quality and microarchitecture outcomes can provide important information regarding bone adaptations during growth. In addition, bone turnover markers can provide further information on cellular bone responses (Jurimae, Maestu, and Jurimae 2010). In parallel with the findings for BMD and BMC, the geometrical adaptations examined by HSA at the narrow neck of the femoral neck also supported a higher bone geometry in footballers (Vlachopoulos, Barker, Williams, et al. 2017). The study used HSA software analysis at the narrow neck of the femur and reported that male adolescent footballers had a significantly larger cross-sectional moment of inertia (CSMI) (17 %), cross-sectional area (CSA) (19 %), section modulus (21 %) and hip strength index (39 %) than controls. Additionally, using QUS analysis footballers demonstrated higher bone stiffness than controls in the dominant foot (20.1 %) as well as in the non-dominant foot (12.9 %), while footballer showed no significant differences between the dominant vs. non-dominant foot (Vlachopoulos, Barker, Williams, et al. 2017). A study in oligomenorrheic female athletes reported that engagement in weight-bearing sports for 4 hours per week resulted in significantly higher HSA outcomes compared to non-athletes (Ackerman et al. 2013), which is consistent with the improved structural rigidity previously found in footballers. In a study of adolescent female athletes, greater increase in subperiosteal width was observed in footballers compared to swimmers, while the endocortical diameter was significantly reduced in swimmers after 8 months of training (Ferry et al. 2013). The differences observed in bone mass between osteogenic and non-osteogenic sports (i.e. football vs. swimming) are likely to be explained by differences in the specific mechanical loading pattern on the skeleton (Greene and Naughton 2006). Falk et al. using QUS analysis found that children- and adolescent male

football players had higher values of speed of sound (SOS) than controls (Falk et al. 2010). Madic et al. also compared QUS between footballers and controls and found that footballers had significantly higher SOS values at right and left calcaneus sites than control (Madic et al. 2010). The only cross-sectional study using pQCT to compare dominant and non-dominant bone geometry in adolescent male footballers conducted by Anliker et al. and found that footballers had higher bone mass and improved geometry at 4% of distal tibia, 14 % and 38% of diaphyseal tibia in the non-dominant leg than the dominant leg (Anliker, Sonderegger, and Toigo 2013). These differences between dominant and non-dominant legs might be explained by the higher ground reaction forces experienced by the non-dominant leg when kicks and tackles are performed by the dominant leg (Seabra et al. 2013).

### **3.3 Football participation for promotion bone health in adulthood**

#### **3.2.1 Cross-sectional studies on football and bone health in adulthood**

Football participation can be beneficial for bone health across the ages of adulthood and evidence suggests that the football participation can improve or maintain bone outcomes (Helge, Andersen, et al. 2014, Hagman et al. 2018, Jackman et al. 2013, Krstrup et al. 2010, Helge et al. 2010). A recent systematic review examined the health benefits of recreational football in middle-aged and older adults and concluded that recreational football can be considered an alternative exercise modality for untrained, healthy or unhealthy middle-aged and older adults of both sexes to maintain an active lifestyle and mitigate a wide array of physical and physiological age-related changes (Luo et al. 2018). A cross-sectional study compared BMD of footballers and long-distance runners aged 20-30 years old and showed that leg and calcaneal BMD was significantly higher in football players than controls. Additionally,

footballers had significantly higher right hip and spine BMD than runners, and runners had higher calcaneal BMD than controls (Fredericson et al. 2007). A previous study in 22.3 year old footballers who had been playing football for the last 12 years found a 13-24 % higher BMC than in non-active controls (Calbet et al. 2001), indicating the long-term potential benefits of football participation on bone health. A cross-sectional evaluation in adults showed that participation in repeated moderate impact loading sports may result in lower TBS at the lumbar spine and increased fracture risk compared to high-impact loading sports (Heinio, Nikander, and Sievanen 2015). Another cross-sectional study comparing bone geometry estimates using hip structural analysis in 22 year old female football players and sedentary controls found that total hip BMD, femoral neck BMD and HSA parameters (7-17%) were significantly higher in football players compared to controls after adjusting for body weight (El Hage 2013). Exercises that involve maximal muscle contractions and rapid accelerations and decelerations can place substantial loads on bones and stimulate an increase in bone strength even during adulthood (Schoenau and Frost 2002), which might explain the findings of the previous studies. A recent study has shown that BMD of the proximal femur and total body BMD were significantly higher in lifelong trained male football players aged 65–80 years and young elite football players aged 18–30 years compared to age-matched untrained men. Interestingly, elderly football players even had significantly higher BMD in femoral trochanter and leg BMD than untrained young males despite an age difference of 47 year. It should be noted that adjustments for lean mass and height have been done as part of the study (Hagman et al. 2018).

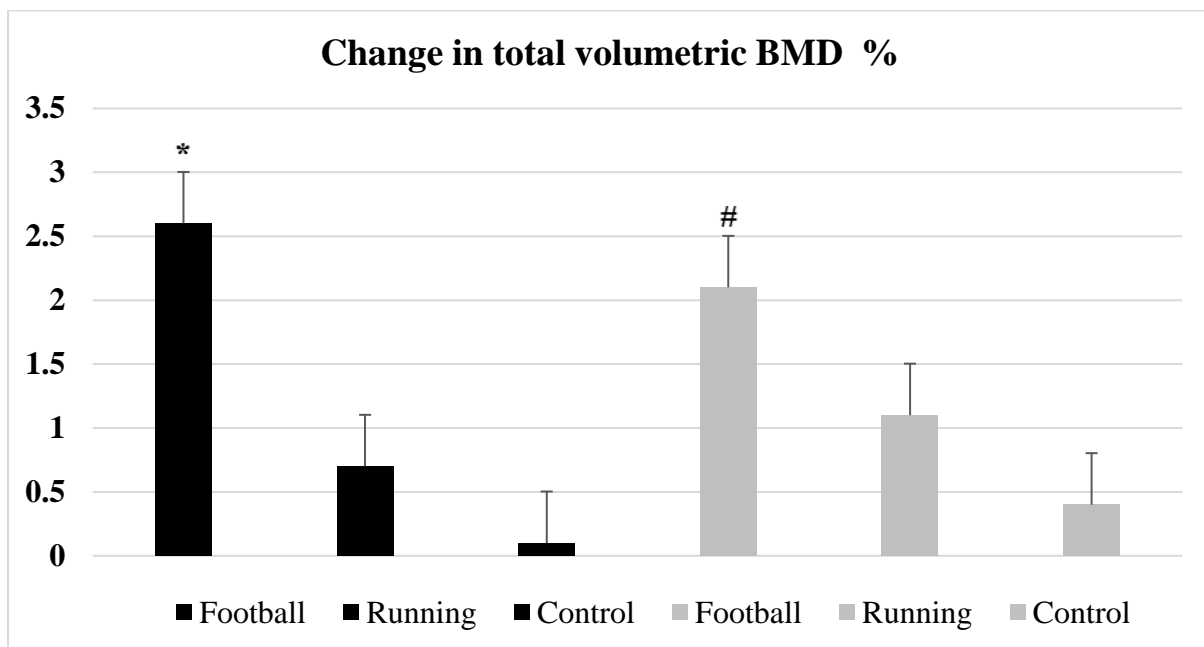
### **3.3.2 Acute and long terms skeletal adaptations from football in adulthood**

The effect of football participation on BMD during adulthood and in elderly populations was investigated by randomised controlled trials that reported small site-specific

skeletal benefits (Helge et al. 2010, Krstrup et al. 2009, Randers et al. 2010). The effect of 14 weeks of recreational football and endurance running on volumetric BMD and muscle power was investigated in untrained premenopausal women aged 36.5 years and compared with a control group. The findings showed that volumetric BMD in left and right tibia increased significantly by 2.6 % and 2.1 % respectively in footballers and by 0.7 % and 1.1 % respectively in runners (**Figure 2**), without any significant changes in controls (Helge et al. 2010). However, no significant improvements were observed in areal BMD at any skeletal sites of the groups, possibly due to the short duration of the programme. Additionally, significant improvements were observed in the football group in peak jump power by 3 %, hamstring strength during fast (240°/s) and slow (30°/s) contractions by 11 % and 9 % respectively, but there were no significant improvements in the endurance running and control groups (Helge et al. 2010). These findings highlight the potential of a 14-week football training programme (1.8 hours per week) to significantly improve peak jump power, maximal hamstring strength and volumetric BMD in premenopausal women that could potentially decrease the risk of falling and fracture. Similarly, a 16-week football training study in elite and untrained young women aged 24 years showed that at baseline total and leg BMD and BMC were 13-24 % and 23-28 % significantly higher in the elite group compared to the untrained group. After 16 weeks of football training for the untrained group, lean body mass was significantly increased by 1.4 kg and the number of falls was decreased by 29%, but no significant changes occurred in BMD or BMC (Jackman et al. 2013). A study compared the effect of recreational football and running for 12 weeks on BMD in 20–43-year-old sedentary men. The results showed that total body BMD was not significantly increased in any group, while lower-extremity BMD was increased by 2 % following the 12-week short-term soccer training, but unaltered in the running group. The increase in lean body mass and lower-extremity bone mass over 12 weeks were greater in the football group than in runners and controls, with no significant difference between runners



and controls (Krustrup et al. 2009). A different study in untrained adult males that measured at baseline, at 12 weeks and at 52 weeks showed that the BMD and the BMC at the legs was significantly higher (2.0 and 3.5 %, respectively) at 52 weeks, but it was not different at baseline and at 12 weeks (Randers et al. 2010). It is likely that the movement characteristics in the football group, include many changes of direction and jumps, which can augment BMD after a period of training, since the osteogenic stimulus from exercise depends on the strain rate and magnitude induced by muscle contraction and ground reaction forces (Kohrt, Barry, and Schwartz 2009).



**Figure 2.** Percentage change in total volumetric BMD in distal tibia for untrained premenopausal women after 14 weeks of training football (n=12), running (n=16) and an inactive lifestyle (n=9). Results from the left leg are shown in black and results from the right leg in grey. Means  $\pm$  standard deviation. \* denotes significant difference from running and control groups ( $P < 0.05$ ), # denotes significant difference from control group ( $P < 0.05$ ). Adapted from (Helge et al. 2010).

### 3.3.3 Football participation and cellular bone adaptations in adulthood

The positive effects of football participation can also be seen in the cellular level of bones by using bone turnover markers, such as osteocalcin and N-terminal propeptide of type 1 procollagen (P1NP) as bone formation markers, and C-terminal telopeptide of type 1 collagen (CTX) as a bone resorption marker. A 15-week study in sedentary women aged 45 years showed that football training can improve bone turnover marker profile, while swimming training did not have similar effects (Mohr et al. 2015). Specifically, it was found that osteocalcin and P1NP significantly increased by 37 % and 42 % respectively in the football training group, whereas no increases were observed in the high-intensity intermittent, moderate-intensity swimming and the control group. Additionally, in the football group leg BMC significantly increased by 3.1 %, and BMD in the femoral shaft and trochanter significantly increased by 1.7 % and 2.4 % respectively. There was not observed any increases in the other groups over 15-weeks. A longer duration study investigated the effects of effect of 12 months of recreational football and resistance training on BMD and bone turnover markers in elderly men 68.2 years. In footballers BMD in proximal femur significantly increased by 1.8 % from 0 to 4 months and by 5.4 % from 0 to 12 months, while total body BMD remained unchanged. After 4 and 12 months of football, osteocalcin was increased by 45 % and 46 % from baseline, and P1NP was 41 % and 40 % higher from baseline. CTX only increased after 12 months by 43 % from baseline. In resistance training and controls, BMD and bone turnover markers remained unchanged. These findings indicate that an osteogenic adaptation was initiated after 4 months of recreational football for elderly men, which was further increased after 12 months, while the resistance training group did not have similar improvements (Helge, Andersen, et al. 2014). These findings suggest that the osteogenic BMD response in elderly men is not lower, but rather slower, than in their younger counterparts. Measurements of biochemical bone turnover markers in the elderly suggested that the anabolic response might be due to the improvements in P1NP but not in CTX. The changes in the elderly population are

higher than what has been observed in other intervention studies examining the skeletal effect of physical activity (Vincent and Braith 2002, Bolam, van Uffelen, and Taaffe 2013). The effects of football participation on bone metabolism were also investigated by a case-control study in homeless men who were monitored over 12 weeks, and the findings showed that osteocalcin increased by 27% along with minor improvements (1.0%) in trunk BMD (Helge, Randers, et al. 2014). Another mechanistic study compared the acute effects of a short-duration vibration exercise session and two football sessions of respectively 15 minutes and 1 hour duration on bone turnover markers. The findings revealed that 48 h after a single bout of exercise, plasma osteocalcin concentration increased by 10 % in all groups, whereas P1NP increased by 15% after 15 minutes of small-sided football training, whereas P1NP failed to increase in the short-duration vibration group (Bowtell et al. 2016). These findings indicate that the observed beneficial effects of football participation may to some extent be attributable to the repeated stimulation of osteoblast activity within each single training session.

### **3.4 Conclusions**

Football is the most popular sport practised worldwide and there is conclusive evidence that football participation has site-specific positive effects on skeletal bone mass during growth and in adulthood. The positive effects of football participation during pubertal might be greater than year compared to pre or post pubertal years partially due to the rapid increases of sex and growth hormones that have an independent effect on bone accretion in that period. Additionally participation in football for more years starting from childhood might induce greater adaptations due to the greater exposure to weight-bearing loadings which might lead to more pronounced bone development. The benefits of football practise are observed in both male and female athletes during growth and in adulthood with evidence indicating structural, cellular

and clinical relevant bone adaptations. During adulthood football can be considered an effective exercise modality to not only maintain but also improve bone health in untrained middle-aged and older men and women including clinical patient groups. The skeletal benefits are site-specific with lower limbs skeletal regions, such as hip, femoral neck, trochanter, and intertrochanteric, being particularly stimulated by the mechanical loads elicited by football specific movements, such as jumps, changes of direction and vigorous accelerations and decelerations. Due to the paucity and variation in quality of available studies, future research should comprise additional high-quality randomised controlled trials and longitudinal studies to establish more in-depth evidence on the positive effects of football practise in childhood, adolescence and mature adulthood. Considerations about research focusing on football and bone health should include the use of important covariates, such as lean body mass and size and the justification of covariates selected in the statistical models. Future applied research should focus on providing evidence on the dose-response relationship for inducing positive bone adaptations during developmental growth and in adulthood in order to allow global policy stakeholders to incorporate football as an effective and feasible sports medicine strategy across the entire lifespan.

### **Please ensure**

You close your chapter will with all or at least a number of the following within your conclusion guidance on recommendations for

- (i) future applied practice and/or intervention implementation
- (ii) future research,
- (iii) considerations for intervention evaluation, and
- (iv) local, regional, national or global policy

## References

- Ackerman, K. E., L. Pierce, G. Guereca, M. Slattery, H. Lee, M. Goldstein, and M. Misra. 2013. "Hip Structural Analysis in Adolescent and Young Adult Oligoamenorrheic and Eumenorrheic Athletes and Nonathletes." *Journal of Clinical Endocrinology & Metabolism* 98 (4):1742-1749. doi: 10.1210/jc.2013-1006.
- Agostinete, R. R., K. R. Lynch, L. A. Gobbo, M. C. Lima, I. H. Ito, R. Luiz-de-Marco, M. A. Rodrigues-Junior, and R. A. Fernandes. 2016. "Basketball Affects Bone Mineral Density Accrual in Boys More Than Swimming and Other Impact Sports: 9-mo Follow-Up." *J Clin Densitom*. doi: 10.1016/j.jocd.2016.04.006.
- Anliker, E., A. Sonderegger, and M. Toigo. 2013. "Side-to-side differences in the lower leg muscle-bone unit in male soccer players." *Med Sci Sports Exerc* 45 (8):1545-52. doi: 10.1249/MSS.0b013e31828cb712.
- Ara, I., G. Vicente-Rodriguez, J. Perez-Gomez, J. Jimenez-Ramirez, J. A. Serrano-Sanchez, C. Dorado, and J. A. Calbet. 2006. "Influence of extracurricular sport activities on body composition and physical fitness in boys: a 3-year longitudinal study." *Int J Obes (Lond)* 30 (7):1062-71. doi: 10.1038/sj.ijo.0803303.
- Bachrach, L. K. 2001. "Acquisition of optimal bone mass in childhood and adolescence." *Trends Endocrinol Metab* 12 (1):22-8.
- Bass, S. L., L. Saxon, R. M. Daly, C. H. Turner, A. G. Robling, E. Seeman, and S. Stuckey. 2002. "The effect of mechanical loading on the size and shape of bone in pre-, peri-, and postpubertal girls: a study in tennis players." *J Bone Miner Res* 17 (12):2274-80. doi: 10.1359/jbmr.2002.17.12.2274.
- Baxter-Jones, A. D., R. A. Faulkner, M. R. Forwood, R. L. Mirwald, and D. A. Bailey. 2011. "Bone mineral accrual from 8 to 30 years of age: an estimation of peak bone mass." *J Bone Miner Res* 26 (8):1729-39. doi: 10.1002/jbmr.412.
- Bolam, K. A., J. G. van Uffelen, and D. R. Taaffe. 2013. "The effect of physical exercise on bone density in middle-aged and older men: a systematic review." *Osteoporos Int* 24 (11):2749-62. doi: 10.1007/s00198-013-2346-1.
- Bonjour, Jean-Philippe, and Thierry Chevalley. 2007. "Pubertal timing, peak bone mass and fragility fracture risk." *BoneKEy-Osteovision* 4 (2):30-48. doi: 10.1138/20060247.
- Boonen, S., R. F. Laan, I. P. Barton, and N. B. Watts. 2005. "Effect of osteoporosis treatments on risk of non-vertebral fractures: review and meta-analysis of intention-to-treat studies." *Osteoporos Int* 16 (10):1291-8. doi: 10.1007/s00198-005-1945-x.
- Bowtell, J. L., S. R. Jackman, S. Scott, L. J. Connolly, M. Mohr, G. Ermidis, R. Julian, F. Yousefian, E. W. Helge, N. R. Jorgensen, J. Fulford, K. M. Knapp, and P. Krstrup. 2016. "Short Duration Small Sided Football and to a Lesser Extent Whole Body Vibration Exercise Induce Acute Changes in Markers of Bone Turnover." *Biomed Res Int* 2016:3574258. doi: 10.1155/2016/3574258.
- Calbet, J. A., C. Dorado, P. Diaz-Herrera, and L. P. Rodriguez-Rodriguez. 2001. "High femoral bone mineral content and density in male football (soccer) players." *Med Sci Sports Exerc* 33 (10):1682-7.
- Courteix, D., C. Jaffre, E. Lespessailles, and L. Benhamou. 2005. "Cumulative effects of calcium supplementation and physical activity on bone accretion in premenarchal children: a double-blind randomised placebo-controlled trial." *Int J Sports Med* 26 (5):332-8. doi: 10.1055/s-2004-821040.
- Courteix, D., E. Lespessailles, S. L. Peres, P. Obert, P. Germain, and C. L. Benhamou. 1998. "Effect of physical training on bone mineral density in prepubertal girls: A comparative study between impact-loading and non-impact-loading sports." *Osteoporosis International* 8 (2):152-158. doi: Doi 10.1007/Bf02672512.

- Dowthwaite, J. N., P. F. Rosenbaum, and T. A. Scerpella. 2012. "Site-specific advantages in skeletal geometry and strength at the proximal femur and forearm in young female gymnasts." *Bone* 50 (5):1173-83. doi: 10.1016/j.bone.2012.01.022.
- Duncan, C. S., C. J. Blimkie, C. T. Cowell, S. T. Burke, J. N. Briody, and R. Howman-Giles. 2002. "Bone mineral density in adolescent female athletes: relationship to exercise type and muscle strength." *Med Sci Sports Exerc* 34 (2):286-94.
- Dvorak, J., and A. Junge. 2015. "Twenty years of the FIFA Medical Assessment and Research Centre: from 'medicine for football' to 'football for health'." *Br J Sports Med* 49 (9):561-3. doi: 10.1136/bjsports-2015-094805.
- El Hage, R. 2013. "Geometric indices of hip bone strength in young female football players." *Journal of Musculoskeletal & Neuronal Interactions* 13 (2):206-212.
- Falk, B., S. Braid, M. Moore, M. Yao, P. Sullivan, and N. Klentrou. 2010. "Bone properties in child and adolescent male hockey and soccer players." *J Sci Med Sport* 13 (4):387-91. doi: 10.1016/j.jsams.2009.03.011.
- Faulkner, R. A., and D. A. Bailey. 2007. "Osteoporosis: a pediatric concern?" *Med Sport Sci* 51:1-12. doi: 10.1159/0000102993.
- Faulkner, R. A., M. R. Forwood, T. J. Beck, J. C. Mafukidze, K. Russell, and W. Wallace. 2003. "Strength indices of the proximal femur and shaft in prepubertal female gymnasts." *Med Sci Sports Exerc* 35 (3):513-8. doi: 10.1249/01.MSS.0000053724.33480.8B.
- Ferry, B., M. Duclos, L. Burt, P. Therre, F. Le Gall, C. Jaffre, and D. Courteix. 2011. "Bone geometry and strength adaptations to physical constraints inherent in different sports: comparison between elite female soccer players and swimmers." *J Bone Miner Metab* 29 (3):342-51. doi: 10.1007/s00774-010-0226-8.
- Ferry, B., E. Lespessailles, P. Rochcongar, M. Duclos, and D. Courteix. 2013. "Bone health during late adolescence: effects of an 8-month training program on bone geometry in female athletes." *Joint Bone Spine* 80 (1):57-63. doi: 10.1016/j.jbspin.2012.01.006.
- Fredericson, M., K. Chew, J. Ngo, T. Cleek, J. Kiratli, and K. Cobb. 2007. "Regional bone mineral density in male athletes: a comparison of soccer players, runners and controls." *Br J Sports Med* 41 (10):664-8; discussion 668. doi: 10.1136/bjism.2006.030783.
- Gordon, C. M., B. S. Zemel, T. A. Wren, M. B. Leonard, L. K. Bachrach, F. Rauch, V. Gilsanz, C. J. Rosen, and K. K. Winer. 2017. "The Determinants of Peak Bone Mass." *J Pediatr* 180:261-269. doi: 10.1016/j.jpeds.2016.09.056.
- Greene, D. A., and G. A. Naughton. 2006. "Adaptive skeletal responses to mechanical loading during adolescence." *Sports Med* 36 (9):723-32.
- Hagman, M., E. W. Helge, T. Hornstrup, B. Frstrup, J. J. Nielsen, N. R. Jorgensen, J. L. Andersen, J. W. Helge, and P. Krstrup. 2018. "Bone mineral density in lifelong trained male football players compared with young and elderly untrained men." *Journal of Sport and Health Science* 7 (2):159-168. doi: 10.1016/j.jshs.2017.09.009.
- Heinio, L., R. Nikander, and H. Sievanen. 2015. "Association between long-term exercise loading and lumbar spine trabecular bone score (TBS) in different exercise loading groups." *Journal of Musculoskeletal & Neuronal Interactions* 15 (3):279-285.
- Helge, E. W., P. Aagaard, M. D. Jakobsen, E. Sundstrup, M. B. Randers, M. K. Karlsson, and P. Krstrup. 2010. "Recreational football training decreases risk factors for bone fractures in untrained premenopausal women." *Scand J Med Sci Sports* 20 Suppl 1:31-9. doi: 10.1111/j.1600-0838.2010.01107.x.
- Helge, E. W., T. R. Andersen, J. F. Schmidt, N. R. Jorgensen, T. Hornstrup, P. Krstrup, and J. Bangsbo. 2014. "Recreational football improves bone mineral density and bone turnover marker profile in elderly men." *Scandinavian Journal of Medicine & Science in Sports* 24:98-104. doi: 10.1111/sms.12239.
- Helge, E. W., M. B. Randers, T. Hornstrup, J. J. Nielsen, J. Blackwell, S. R. Jackman, and P. Krstrup. 2014. "Street football is a feasible health-enhancing activity for homeless men: Biochemical

- bone marker profile and balance improved." *Scandinavian Journal of Medicine & Science in Sports* 24:122-129. doi: 10.1111/sms.12244.
- Henry, Y. M., D. Fatayerji, and R. Eastell. 2004. "Attainment of peak bone mass at the lumbar spine, femoral neck and radius in men and women: relative contributions of bone size and volumetric bone mineral density." *Osteoporos Int* 15 (4):263-73. doi: 10.1007/s00198-003-1542-9.
- Hernlund, E., A. Svedbom, M. Ivergard, J. Compston, C. Cooper, J. Stenmark, E. V. McCloskey, B. Jonsson, and J. A. Kanis. 2013. "Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA)." *Arch Osteoporos* 8:136. doi: 10.1007/s11657-013-0136-1.
- Hind, K., and M. Burrows. 2007. "Weight-bearing exercise and bone mineral accrual in children and adolescents: a review of controlled trials." *Bone* 40 (1):14-27. doi: 10.1016/j.bone.2006.07.006.
- Hind, K., L. Gannon, E. Whatley, C. Cooke, and J. Truscott. 2012. "Bone cross-sectional geometry in male runners, gymnasts, swimmers and non-athletic controls: a hip-structural analysis study." *Eur J Appl Physiol* 112 (2):535-41. doi: 10.1007/s00421-011-2008-y.
- Jackman, S. R., S. Scott, M. B. Randers, C. Orntoft, J. Blackwell, A. Zar, E. W. Helge, M. Mohr, and P. Krstrup. 2013. "Musculoskeletal health profile for elite female footballers versus untrained young women before and after 16 weeks of football training." *Journal of Sports Sciences* 31 (13):1468-1474. doi: 10.1080/02640414.2013.796066.
- Johnell, O., and J. A. Kanis. 2006. "An estimate of the worldwide prevalence and disability associated with osteoporotic fractures." *Osteoporos Int* 17 (12):1726-33. doi: 10.1007/s00198-006-0172-4.
- Jurimae, J., J. Maestu, and T. Jurimae. 2010. "Bone turnover markers during pubertal development: relationships with growth factors and adipocytokines." *Med Sport Sci* 55:114-27. doi: 10.1159/000321976.
- Kanis, J. A., N. Burlet, C. Cooper, P. D. Delmas, J. Y. Reginster, F. Borgstrom, and R. Rizzoli. 2008. "European guidance for the diagnosis and management of osteoporosis in postmenopausal women." *Osteoporos Int* 19 (4):399-428.
- Kanis, J. A., and O. Johnell. 2005. "Requirements for DXA for the management of osteoporosis in Europe." *Osteoporos Int* 16 (3):229-38.
- Kinsella, K., and H. Wan. 2008. "International population reports, P95/09-1, an aging world: 2008." *US Census Bureau, US Government Printing Office, Washington, DC (2009)*.
- Kohrt, W. M., D. W. Barry, and R. S. Schwartz. 2009. "Muscle Forces or Gravity: What Predominates Mechanical Loading on Bone?" *Medicine and Science in Sports and Exercise* 41 (11):2050-2055. doi: 10.1249/MSS.0b013e3181a8c717.
- Krstrup, P., P. R. Hansen, L. J. Andersen, M. D. Jakobsen, E. Sundstrup, M. B. Randers, L. Christiansen, E. W. Helge, M. T. Pedersen, P. Sogaard, A. Junge, J. Dvorak, P. Aagaard, and J. Bangsbo. 2010. "Long-term musculoskeletal and cardiac health effects of recreational football and running for premenopausal women." *Scand J Med Sci Sports* 20 Suppl 1:58-71. doi: 10.1111/j.1600-0838.2010.01111.x.
- Krstrup, P., J. J. Nielsen, B. R. Krstrup, J. F. Christensen, H. Pedersen, M. B. Randers, P. Aagaard, A. M. Petersen, L. Nybo, and J. Bangsbo. 2009. "Recreational soccer is an effective health-promoting activity for untrained men." *British Journal of Sports Medicine* 43 (11):825-831. doi: 10.1136/bjsm.2008.053124.
- Lappe, J. M., P. Watson, V. Gilsanz, T. Hangartner, H. J. Kalkwarf, S. Oberfield, J. Shepherd, K. K. Winer, and B. Zemel. 2014. "The Longitudinal Effects of Physical Activity and Dietary Calcium on Bone Mass Accrual Across Stages of Pubertal Development." *J Bone Miner Res*. doi: 10.1002/jbmr.2319.

- Larsen, M. N., C. M. Nielsen, E. W. Helge, M. Madsen, V. Manniche, L. Hansen, P. R. Hansen, J. Bangsbo, and P. Krstrup. 2018. "Positive effects on bone mineralisation and muscular fitness after 10 months of intense school-based physical training for children aged 8-10 years: the FIT FIRST randomised controlled trial." *British Journal of Sports Medicine* 52 (4):254-+. doi: 10.1136/bjsports-2016-096219.
- Lozano-Berges, G., A. Matute-Llorente, A. Gonzalez-Aguero, A. Gomez-Bruton, A. Gomez-Cabello, G. Vicente-Rodriguez, and J. A. Casajus. 2018. "Soccer helps build strong bones during growth: a systematic review and meta-analysis." *Eur J Pediatr* 177 (3):295-310. doi: 10.1007/s00431-017-3060-3.
- Luo, Hao, Robert U Newton, Fadi Ma'ayah, Daniel A Galvão, and Dennis R Taaffe. 2018. "Recreational soccer as sport medicine for middle-aged and older adults: a systematic review." *BMJ Open Sport & Exercise Medicine* 4 (1). doi: 10.1136/bmjsem-2017-000336.
- Madic, D., B. Obradovic, M. Smajic, J. Obradovic, D. Maric, and K. Boskovic. 2010. "Status of bone mineral content and body composition in boys engaged in intensive physical activity." *Vojnosanit Pregl* 67 (5):386-90.
- Maimoun, L., O. Coste, T. Mura, P. Philibert, F. Galtier, D. Mariano-Goulart, F. Paris, and C. Sultan. 2013. "Specific bone mass acquisition in elite female athletes." *J Clin Endocrinol Metab* 98 (7):2844-53. doi: 10.1210/jc.2013-1070.
- Melton, L. J., E. A. Chrischilles, C. Cooper, A. W. Lane, and B. L. Riggs. 1992. "How Many Women Have Osteoporosis." *Journal of Bone and Mineral Research* 7 (9):1005-1010.
- Mitchell, J. A., A. Chesi, O. Elci, S. E. McCormack, H. J. Kalkwarf, J. M. Lappe, V. Gilsanz, S. E. Oberfield, J. A. Shepherd, A. Kelly, B. S. Zemel, and S. F. Grant. 2015. "Genetics of Bone Mass in Childhood and Adolescence: Effects of Sex and Maturation Interactions." *J Bone Miner Res* 30 (9):1676-83. doi: 10.1002/jbmr.2508.
- Mohr, M., E. W. Helge, L. F. Petersen, A. Lindenskov, P. Weihe, J. Mortensen, N. R. Jorgensen, and P. Krstrup. 2015. "Effects of soccer vs swim training on bone formation in sedentary middle-aged women." *European Journal of Applied Physiology* 115 (12):2671-2679. doi: 10.1007/s00421-015-3231-8.
- Mouratidou, T., G. Vicente-Rodriguez, L. Gracia-Marco, I. Huybrechts, I. Sioen, K. Widhalm, J. Valtuena, M. Gonzalez-Gross, L. A. Moreno, and Helena Study Group. 2013. "Associations of dietary calcium, vitamin D, milk intakes, and 25-hydroxyvitamin D with bone mass in Spanish adolescents: the HELENA study." *J Clin Densitom* 16 (1):110-7. doi: 10.1016/j.jocd.2012.07.008.
- Nebigh, A., H. Rebai, M. Elloumi, A. Bahlous, M. Zouch, M. Zaouali, C. Alexandre, S. Sellami, and Z. Tabka. 2009. "Bone mineral density of young boy soccer players at different pubertal stages: relationships with hormonal concentration." *Joint Bone Spine* 76 (1):63-9. doi: 10.1016/j.jbspin.2008.03.002.
- NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. 2001. "Osteoporosis prevention, diagnosis, and therapy." *JAMA* 285 (6):785-95.
- Nikander, R., H. Sievanen, A. Heinonen, and P. Kannus. 2005. "Femoral neck structure in adult female athletes subjected to different loading modalities." *J Bone Miner Res* 20 (3):520-8. doi: 10.1359/JBMR.041119.
- Randell, A., P. N. Sambrook, T. V. Nguyen, H. Lapsley, G. Jones, P. J. Kelly, and J. A. Eisman. 1995. "Direct clinical and welfare costs of osteoporotic fractures in elderly men and women." *Osteoporosis International* 5 (6):427-432. doi: Doi 10.1007/Bf01626603.
- Randers, M. B., J. J. Nielsen, B. R. Krstrup, E. Sundstrup, M. D. Jakobsen, L. Nybo, J. Dvorak, J. Bangsbo, and P. Krstrup. 2010. "Positive performance and health effects of a football training program over 12 weeks can be maintained over a 1-year period with reduced training frequency." *Scandinavian Journal of Medicine & Science in Sports* 20:80-89. doi: 10.1111/j.1600-0838.2010.01091.x.



- Reginster, J. Y., and N. Burlet. 2006. "Osteoporosis: A still increasing prevalence." *Bone* 38 (2):4-9. doi: 10.1016/j.bone.2005.11.024.
- Schoenau, E., and H. M. Frost. 2002. "The "muscle-bone unit" in children and adolescents." *Calcified Tissue International* 70 (5):405-407. doi: 10.1007/s00223-001-0048-8.
- Seabra, A. F., J. Brito, E. Marques, S. Abreu, J. Oliveira, J. Mota, P. Krstrup, C. Rego, and A. Rebelo. 2013. "Muscle Strength And Soccer Practice As Major Determinants Of Bone Mineral Density In Adolescents." *Medicine and Science in Sports and Exercise* 45 (5):107-107.
- Silva, C. C., T. B. Goldberg, A. S. Teixeira, and J. C. Dalmas. 2011. "The impact of different types of physical activity on total and regional bone mineral density in young Brazilian athletes." *J Sports Sci* 29 (3):227-34. doi: 10.1080/02640414.2010.529456.
- Stewart, T. L., and S. H. Ralston. 2000. "Role of genetic factors in the pathogenesis of osteoporosis." *J Endocrinol* 166 (2):235-45.
- Theintz, G., B. Buchs, R. Rizzoli, D. Slosman, H. Clavien, P. C. Sizonenko, and J. P. Bonjour. 1992. "Longitudinal monitoring of bone mass accumulation in healthy adolescents: evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects." *J Clin Endocrinol Metab* 75 (4):1060-5. doi: 10.1210/jcem.75.4.1400871.
- Torres-Costoso, A., D. Vlachopoulos, E. Ubago-Guisado, A. Ferri-Morales, I. Caverro-Redondo, V. Martinez-Vizcaino, and L. Gracia-Marco. 2018. "Agreement Between Dual-Energy X-Ray Absorptiometry and Quantitative Ultrasound to Evaluate Bone Health in Adolescents: The PRO-BONE Study." *Pediatr Exerc Sci*:1-8. doi: 10.1123/pes.2017-0217.
- Tournis, S., E. Michopoulou, I. G. Fatouros, I. Paspatis, M. Michalopoulou, P. Raptou, D. Leontsini, A. Avloniti, M. Krekoulia, V. Zouvelou, A. Galanos, N. Aggelousis, A. Kambas, I. Douroudos, G. P. Lyritis, K. Taxildaris, and N. Pappaioannou. 2010. "Effect of Rhythmic Gymnastics on Volumetric Bone Mineral Density and Bone Geometry in Premenarcheal Female Athletes and Controls." *Journal of Clinical Endocrinology & Metabolism* 95 (6):2755-2762. doi: 10.1210/jc.2009-2382.
- Turner, C. H. 1998. "Three rules for bone adaptation to mechanical stimuli." *Bone* 23 (5):399-407.
- Uth, J., B. Frstrup, R. D. Haahr, K. Brasso, J. W. Helge, M. Rorth, J. Midtgaard, E. W. Helge, and P. Krstrup. 2018. "Football training over 5 years is associated with preserved femoral bone mineral density in men with prostate cancer." *Scandinavian Journal of Medicine & Science in Sports* 28:61-73. doi: 10.1111/sms.13242.
- Valtuna, J., L. Gracia-Marco, G. Vicente-Rodriguez, M. Gonzalez-Gross, I. Huybrechts, J. P. Rey-Lopez, T. Mouratidou, I. Sioen, M. I. Mesana, A. E. Martinez, K. Widhalm, L. A. Moreno, and Helena Study Group. 2012. "Vitamin D status and physical activity interact to improve bone mass in adolescents. The HELENA Study." *Osteoporos Int* 23 (8):2227-37. doi: 10.1007/s00198-011-1884-7.
- Vanderschueren, D., L. Vandenput, and S. Boonen. 2005. "Reversing sex steroid deficiency and optimizing skeletal development in the adolescent with gonadal failure." *Endocr Dev* 8:150-65. doi: 10.1159/000084100.
- Vicente-Rodriguez, G., I. Ara, J. Perez-Gomez, C. Dorado, and J. A. Calbet. 2005. "Muscular development and physical activity as major determinants of femoral bone mass acquisition during growth." *Br J Sports Med* 39 (9):611-6. doi: 10.1136/bjsm.2004.014431.
- Vicente-Rodriguez, G., I. Ara, J. Perez-Gomez, J. A. Serrano-Sanchez, C. Dorado, and J. A. Calbet. 2004. "High femoral bone mineral density accretion in prepubertal soccer players." *Med Sci Sports Exerc* 36 (10):1789-95.
- Vicente-Rodriguez, G., J. Jimenez-Ramirez, I. Ara, J. A. Serrano-Sanchez, C. Dorado, and J. A. Calbet. 2003. "Enhanced bone mass and physical fitness in prepubescent footballers." *Bone* 33 (5):853-9.
- Vincent, K. R., and R. W. Braith. 2002. "Resistance exercise and bone turnover in elderly men and women." *Med Sci Sports Exerc* 34 (1):17-23.

- Vlachopoulos, D, L Gracia-Marco, A.R Barker, I Huybrechts, L A Moreno, and T Mouratidou. 2016. "Bone Health: The independent and combined effects of calcium, vitamin D and exercise in children and adolescents." In *Calcium: Chemistry, Analysis, Function and Effects*, edited by V R Preedy, 530-546. London, UK: The Royal Society of Chemistry.
- Vlachopoulos, D., A. R. Barker, E. Ubago-Guisado, I. G. Fatouros, K. M. Knapp, C. A. Williams, and L. Gracia-Marco. 2017. "Longitudinal Adaptations of Bone Mass, Geometry, and Metabolism in Adolescent Male Athletes: The PRO-BONE Study." *J Bone Miner Res* 32 (11):2269-2277. doi: 10.1002/jbmr.3206.
- Vlachopoulos, D., A. R. Barker, E. Ubago-Guisado, F. B. Ortega, P. Krstrup, B. Metcalf, J. C. Pinero, J. R. Ruiz, K. M. Knapp, C. A. Williams, L. A. Moreno, and L. Gracia-Marco. 2018. "The effect of 12-month participation in osteogenic and non-osteogenic sports on bone development in adolescent male athletes. The PRO-BONE study." *Journal of Science and Medicine in Sport* 21 (4):404-409. doi: 10.1018/j.jsams.2017.08.018.
- Vlachopoulos, D., A. R. Barker, C. A. Williams, A. RINGRIMSSON SA, K. M. Knapp, B. S. Metcalf, I. G. Fatouros, L. A. Moreno, and L. Gracia-Marco. 2017. "The Impact of Sport Participation on Bone Mass and Geometry in Male Adolescents." *Med Sci Sports Exerc* 49 (2):317-326. doi: 10.1249/MSS.0000000000001091.
- Vlachopoulos, D., E. Ubago-Guisado, A. R. Barker, B. S. Metcalf, I. G. Fatouros, A. Avloniti, K. M. Knapp, L. A. Moreno, C. A. Williams, and L. Gracia-Marco. 2017. "Determinants of Bone Outcomes in Adolescent Athletes at Baseline: The PRO-BONE Study." *Med Sci Sports Exerc* 49 (7):1389-1396. doi: 10.1249/MSS.0000000000001233.
- Ward, K. A., S. A. Roberts, J. E. Adams, S. Lanham-New, and M. Z. Mughal. 2007. "Calcium supplementation and weight bearing physical activity--do they have a combined effect on the bone density of pre-pubertal children?" *Bone* 41 (4):496-504. doi: 10.1016/j.bone.2007.06.007.
- Ward, K. A., S. A. Roberts, J. E. Adams, and M. Z. Mughal. 2005. "Bone geometry and density in the skeleton of pre-pubertal gymnasts and school children." *Bone* 36 (6):1012-8. doi: 10.1016/j.bone.2005.03.001.
- Weiler, R., R. Keen, and R. Wolman. 2012. "Changes in bone turnover markers during the close season in elite football (soccer) players." *J Sci Med Sport* 15 (3):255-8. doi: 10.1016/j.jsams.2011.09.004.
- Wolff, I., J. J. van Croonenborg, H. C. Kemper, P. J. Kostense, and J. W. Twisk. 1999. "The effect of exercise training programs on bone mass: a meta-analysis of published controlled trials in pre- and postmenopausal women." *Osteoporos Int* 9 (1):1-12.
- Zouch, M., C. Jaffre, T. Thomas, D. Frere, D. Courteix, L. Vico, and C. Alexandre. 2008. "Long-term soccer practice increases bone mineral content gain in prepubescent boys." *Joint Bone Spine* 75 (1):41-9. doi: 10.1016/j.jbspin.2006.12.008.
- Zouch, M., L. Vico, D. Frere, Z. Tabka, and C. Alexandre. 2014. "Young male soccer players exhibit additional bone mineral acquisition during the peripubertal period: 1-year longitudinal study." *Eur J Pediatr* 173 (1):53-61. doi: 10.1007/s00431-013-2115-3.
- Zouch, M., A. Zribi, C. Alexandre, H. Chaari, D. Frere, Z. Tabka, and L. Vico. 2015. "Soccer increases bone mass in prepubescent boys during growth: a 3-yr longitudinal study." *J Clin Densitom* 18 (2):179-86. doi: 10.1016/j.jocd.2014.10.004.